12. MALFORMATIONS OF THE LIMBS AND EXTREMITIES (J1-J7)

In many ways it is unrealistic to consider limb malformations in isolation, because the more carefully many of them are examined, the higher is the proportion that can be shown to be only the most obvious manifestation of a disturbance elsewhere and in particular of the development of the skeleton as a whole. Nevertheless, there are a series of disturbances confined to or mainly manifest in the limbs or only in the hands and feet. Of those, at least half are manifest predominantly as anomalies of the fingers or toes. Many of these anomalies are not of much importance to the individual, but they are of considerable interest in the context of embryology and human biology.

POLYDACTYLY (J1-J3) IN SINGLE BIRTHS

In most parts of the world the commonest individual malformation of the extremities is an extra finger or an extra toe or both, although extra fingers outnumber the sum of the other two. Differentiation of the hand buds is earlier than that of the foot, and it is not surprising that polydactyly of hand and feet frequently occur independently of each other as well as together. Most of this polydactyly is determined by an extra digit on the ulnar side of the hand, varying from a more or less complete digit with nail formation to a rudimentary finger with or without cartilage or a centre of ossification to only a small skin tag. Answers to questions sent to organizers at various centres subsequent to completion of recording make it clear that it is this type of malformation which is probably present in most cases grouped as J3, where " polydactyly " without further description or " hexadactyly " was recorded.

Polydactyly grouped as J1 and J3

In the complete form of ulnar polydactyly there is usually a bony spur on the fifth metacarpal below the metacarpo-phalangeal joint. In other cases there is simply a spur on the fifth metacarpal and/or a rudimentary finger, a skin tag or even a dimple where such a skin tag could have originated. The data from the study relative to these conditions are displayed in Table 12.1

As already indicated it seems likely that those classifiable on recorded descriptions as J1 represent only a minority of all cases of ulnar polydactyly. On the other hand, J3 is a heterogeneous group. At a guess perhaps two-thirds of cases in J3 are ulnar polydactyly but some are of lateral polydactyly of feet or of hands and feet while others may be of uncommon types involving duplication or partial duplication of the middle digits.

There is no significant correlation at a 5% level between the frequencies of J1 and J3 ($r = +0.039$). However, this is not necessarily in conflict with the remarks above, if as is almost certainly true, in some centres most cases of ulnar polydactyly were recorded and therefore grouped by the authors as J1, while in other centres the same condition was simply called " polydactyly " or " hexadactyly " and grouped by the writers as J3. In view of what is known, in spite of the absence of correlation of frequencies, it seems justifiable to group J1 and J3 for some purposes.

Ulnar polydactyly has long been recognized to be very frequent in Africans. In this study the highest frequencies of J1 are in Pretoria (4.79 per 1000), where the patients were all Bantu, and in São Paulo (2.63 per 1000), where there is a large African contribution to the ethnic mixture of many of the mothers. In Pretoria the frequency of J3 was also relatively high. In Panama, where there is also a large African contribution, there were no reported cases described as ulnar polydactyly, but the frequency of J3 was twice as high as in any other centre. From subsequent inquiry it is clear that virtually all cases really were of ulnar polydactyly. From the above it will be clear that it is not possible to judge the real frequencies of ulnar polydactyly, but that the figures for J1 are minimal and those for J1 + J3 maximal as estimates of frequencies.

Most cases of J1 or J3 are sporadic, i.e., occur in only one individual in a family, and the nature of any genetical contribution is unknown. In addition, in many families ulnar polydactyly appears to be inherited by a simple dominant gene mechanism although the condition may not be present in all who are heterozygous for the gene and the manifestation is very variable in those affected. It is sometimes said, presumably on the basis of sporadic cases and

the occasional occurrence in sibs although neither parent is affected, that there is a type determined by a recessive gene mutation. There is no support for such a hypothesis from the present data in that there appears to be no connexion with consanguinity. There is no suggestion of any increase in parental consanguinity in parents of children with polydactyly J1 and J3.

J1 and J3 as one of two or more malformations

Polydactyly occurs as part of a remarkable number of syndromes determined by single genes (for example, Lawrence-Moon-Biedl syndrome, chondro-ectodermal dysplasia and syndromes of the Pierre Robin type), and in those determined by chromosomal abnormalities (e.g., Down's syndrome, trisomy 14/15). It also occurs as one malformation in many infants with multiple malformations where the genetical contribution to etiology, if any, is complex. In all these the polydactyly is almost invariably ulnar or lateral on the feet. Ulnar polydactyly occurs in 25 cases in the N group (7.6%) and there are five cases in that group where there was polydactyly (presumably lateral of both hands and feet).

POLYDACTYLY, RADIAL (J2)

" Radial polydactyly " is strictly a misnomer. In the great majority of cases the condition is simply a duplication of the terminal phalanx of the thumb. A similar condition is found in the great toes. This malformation is much less common in most centres than the ulnar types of polydactyly. Sometimes only the nail is duplex or there is only incomplete duplication of the terminal phalanx. As will be seen from Table 12.1, this condition is less common than J1 and, although a few cases may have been included in J3, it is unlikely that such cases would be described only as polydactyly. Radial polydactyly appears to be more common in Hong Kong (0.91 per 1000 total single births) and Singapore (0.50 per 1000 single births) than elsewhere. In Singapore 19 of 20 cases had Chinese mothers; one was born to an Eurasian. The frequency in Chinese in Singapore is 0.60 per 1000. All four cases in Kuala Lumpur were Chinese—a frequency of 0.46 per 1000. Thus the three highest frequencies are in children of Chinese mothers, which is suggestive. Over all the centres the correlation of the frequencies J1+J3 and J2 is negative ($r=-0.237$). There were six cases where J2 was one of the malformations in the N group.

SYNDACTYLY (J4)

The syndactylies are a complex group. When only two fingers or toes are involved the term is used to include simple webbing at the bases of the digits, fusion of the complete digit except for the bones and what is more properly called symphalangy, where there is bony fusion. Such relatively minor malformations are quite common and indeed some degree of webbing of second and third, or third and fourth toes is so common as hardly to be termed abnormal.

The term is also applied, however, to conditions involving considerable degrees of disorganization of the hand merging into ectrodactyly and often even in lesser degrees than that, but involving absence of another digit. Thus Apert's syndrome is often termed acrocephaly-syndactyly but the syndactyly is really a disorganization of the hand, almost invariably involving the metacarpals as well as the phalanges. Such information as was recorded other than simply syndactyly is set out in the lists of malformations in the Basic Tabulations by Centres booklet.

Both major and minor types of syndactyly occur in some families in a pattern suggesting a single dominant gene hypothesis, and in others as sporadic cases or with a lower familial concentration than compatible with simple Mendelian inheritance. There is no means of making such distinctions from the study data.

Syndactyly also occurs in 10 infants as one of multiple malformations, as is clear from the data considered in section 16. In view of the heterogeneity of types and etiology and particularly in view of the low over-all frequency (0.15 per 1000 single total births), little can be deduced from Table 12.2.

OTHER DIGITAL ANOMALIES (J5)

This is an extremely heterogeneous group, as may be seen from the lists of malformations. There is virtually no limit to the variety of anomalies of differentiation of the digits, so that the various combinations of polydactyly, brachydactyly, syndactyly, symphalangy and absence of digits cannot be classified in any adequate way. As with other anomalies of number and conformation of digits, these anomalies occur as one of several in the same child. In this series one of this group was recorded in 15 cases in the N group (4.5%).

REDUCTION DEFORMITIES OF LIMBS (J6)

There has in recent years been much interest in reduction deformities of limbs since the tragic sequelae of the use of thalidomide in the treatment of early sickness in pregnancy. However, cases which are indistinguishable occur " spontaneously " and there are many varieties of malformation not encountered in thalidomide cases which are conveniently termed reduction deformities.

It is very difficult to decide what to include in such a group apart from so-called " congenital amputations ". Any extremities found on reduced or rudimentary limbs are invariably malformed. If there is agenesis of the radius the ulna is also usually short and the radial side of the hand is malformed. Should these conditions be included? As used here, the term includes absence of any part of a limb, e.g., even a single finger, and it also includes localized brachydactyly. Such terms as " rudimentary arms ", " agenesis hand ", " reduction deformity of . . . ", " phocomelia ", etc., also determined the placing of the case in the J6 category. However, it was very difficult to decide how to classify many cases. This heterogeneous group has a higher frequency than those in the J4 and J5 group (over-all, 0.21 per 1000 total single births). There were 15 cases (0.51 per 1000) from Manila, but the cases appeared not to be of any particular pattern but of all types included in this group. There were eight malformed children classified to the N group in whom a reduction deformity of limbs was one of the malformations.

" OTHER LIMB DEFORMITIES " (J7)

As mentioned above, individual cases posed the problem of grouping in J6 or J7. Radio-ulnar " dysostosis ", " agenesis " or " dysplasia " or Madelung's deformity were included in this group, as were a large variety of conditions such as genu recurvatum and absence of patella. Also included were such conditions as ectrodactyly, genu valgum, flail joints; and odd cases where two or more limb malformations appeared in the same child were retained in this group rather than transferred to group N. A considerable proportion of the variation of numbers between centres is accounted for by " genu recurvatum ".

Twenty-nine cases where one deformity would have determined grouping in J7 have, because there were other malformations, been placed in the N group, and some in which other malformations were skeletal have been placed in the K5 group.

TABLE 12.1

POLYDACTYLY (NOT ASSOCIATED WITH OTHER MALFORMATIONS) (J1-J3) IN SINGLE BIRTHS

CENTRE		Polydactyly (ulnar) (J 1)				All other polydactyly (J 3)				J 1 + J 3				Polydactyly (radial) (J 2)			
		Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births
		M	F	T		M	F	T		M	F	T		M	F	T	
I 1	MELBOURNE	1	1	2	0.25	0	1	1	0.13	1	2	3	0.38	1	0	1	0.13
I 2	MELBOURNE	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-
II	SAO PAULO	18	20	38	2.63	6	3	9	0.62	24	23	47	3.26	0	0	0	-
III	SANTIAGO	5	1	6	0.25	9	4	13	0.55	14	5	19	0.80	0	1	1	0.04
IV 1	BOGOTA	1	1	2	0.11	13	14	27	1.43	14	15	29	1.54	0	0	0	-
IV 2	MEDELLIN	13	10	23	1.12	12	7	19	0.93	25	17	42	2.05	2	2	4	0.20
V	CZECHOSLOVAKIA	5	1	6	0.30	2	2	4	0.20	7	3	10	0.50	2	2	4	0.20
VI	ALEXANDRIA	0	0	0	-	2	1	3	0.31	2	1	3	0.31	0	0	0	-
VII	HONG KONG	0	0	0	-	4	2	6	0.61	4	2	6	0.61	3	6	9	0.91
VIII 1	BOMBAY	3	1	4	0.10	4	6	10	0.25	7	7	14	0.35	0	1	1	0.025
VIII 2	CALCUTTA	0	2	2	0.10	3	2	5	0.26	3	4	7	0.36	0	0	0	-
IX 1	KUALA LUMPUR	2	1	3	0.19	2	0	2	0.13	4	1	5	0.31	1	3	4	0.25
IX 2	SINGAPORE	0	0	0	-	9	6	15	0.38	9	6	15	0.38	10	10	20	0.50
X 1	MEXICO CITY	5	2	7	0.28	12	9	21	0.85	17	11	28	1.13	2	0	2	0.08
X 2	MEXICO CITY	2	1	3	0.21	4	2	6	0.43	6	3	9	0.64	0	0	0	-
XI	BELFAST	0	0	0	-	7	5	12	0.43	7	5	12	0.43	1	1	2	0.07
XII	PANAMA CITY	0	0	0	-	24	24	48	3.03	24	24	48	3.03	0	0	0	-
XIII	MANILA	0	0	0	-	6	1	7	0.24	6	1	7	0.24	3	3	6	0.20
XIV 1	CAPE TOWN	0	2	2	0.66	0	1	1	0.33	0	3	3	0.98	1	0	1	0.33
XIV 2	JOHANNESBURG	3	5	8	0.72	5	2	7	0.63	8	7	15	1.34	1	0	1	0.09
XIV 3	PRETORIA	22	26	48	4.79	8	6	14	1.40	30	32	62	6.18	0	0	0	-
XV	MADRID	1	0	1	0.05	7	7	14	0.71	8	7	15	0.76	0	1	1	0.05
XVI 1	LJUBLJANA	0	0	0	-	2	1	3	0.34	2	1	3	0.34	0	1	1	0.11
XVI 2	ZAGREB	2	0	2	0.24	1	0	1	0.12	3	0	3	0.36	2	0	2	0.24
	TOTAL	83	74	157	0.40	142	106	248	0.59	225	180	405	0.97	29	31	60	0.14

TABLE 12.2
OTHER MALFORMATIONS OF LIMBS AND EXTREMITIES (J4-J7) IN SINGLE BIRTHS

CENTRE		Syndactyly (J 4)				Other digital anomalies (J 5)				Reduction deformities (limbs) (J 6)				Other limb deformities (J 7)			
		Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births
		M	F	T		M	F	T		M	F	T		M	F	T	
I 1	MELBOURNE	3	1	4	0.51	0	0	0	-	0	3	3	0.38	1	1	2	0.25
I 2	MELBOURNE	1	0	1	0.25	0	0	0	-	1	0	1	0.25	3	1	4	1.02
II	SAO PAULO	5	0	5	0.35	0	0	0	-	3	4	7	1.78	3	3	6	0.42
III	SANTIAGO	2	1	3	0.13	0	0	0	-	2	3	5	0.21	2	0	2	0.08
IV 1	BOGOTA	4	2	6	0.32	1	3	4	0.21	4	1	5	0.27	0	4	4	0.21
IV 2	MEDELLIN	2	1	3	0.15	0	3	3	0.15	2	0	2	0.10	1	0	1	0.05
V	CZECHOSLOVAKIA	5	0	5	0.25	7	4	11	0.54	2	1	3	0.15	1	4	5	0.25
VI	ALEXANDRIA	0	0	0	-	0	0	0	-	1	0	1	0.10	0	1	1	0.10
VII	HONG KONG	1	0	1	0.10	1	1	2	0.20	0	0	0	-	0	1	1	0.10
VIII 1	BOMBAY	0	0	0	-	0	1	1	0.03	2	2	4	0.10	11	3	14	0.35
VIII 2	CALCUTTA	0	1	1	0.05	0	0	0	-	1	0	1	0.05	1	4	5	0.26
IX 1	KUALA LUMPUR	0	1	1	0.06	0	2	2	0.12	2	1	3	0.19	2	4	6	0.38
IX 2	SINGAPORE	4	3	7	0.18	0	0	0	-	4	1	5	0.13	8	5	14[a]	0.35
X 1	MEXICO CITY	0	1	1	0.04	2	4	6	0.24	4	4	8	0.32	1	0	1	0.04
X 2	MEXICO CITY	0	0	0	-	1	0	1	0.07	2	2	4	0.28	2	0	2	0.14
XI	BELFAST	4	4	8	0.28	1	4	5	0.18	2	2	4	0.14	5	3	8	0.28
XII	PANAMA CITY	2	0	2	0.13	1	1	2	0.13	1	0	1	0.06	2	2	4	0.25
XIII	MANILA	2	0	2	0.07	4	3	7	0.24	10	5	15	0.51	0	6	6	0.20
XIV 1	CAPE TOWN	0	0	0	-	0	0	0	-	0	1	1	0.33	0	0	0	-
XIV 2	JOHANNESBURG	6	2	8	0.72	2	1	3	0.27	1	0	1	0.09	2	1	3	0.27
XIV 3	PRETORIA	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-
XV	MADRID	2	1	3	0.15	1	0	1	0.05	3	3	6	0.30	0	0	0	-
XVI 1	LJUBLJANA	1	0	1	0.11	0	0	0	-	2	1	3	0.34	0	0	0	-
XVI 2	ZAGREB	1	0	1	0.12	2	1	3	0.36	3	2	5	0.59	0	0	0	-
	TOTAL	45	18	63	0.15	23	28	51	0.12	52	36	88	0.21	45	43	89[a]	0.21

[a] Includes 1 sex not recorded.